

## **Abstract**

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Title of Doctoral Thesis: Analysis of selected risks of pharmacotherapy

## **Abstract**

### **Introduction and aims**

The aim of this study was to describe and analyse selected pharmacotherapy risks in everyday clinical practice. The paper focused on the guidance of the secondary prevention after myocardial infarction (MI), on opinions, attitudes and experience of general practitioners with generic substitution and on self-medication of the elderly in the Czech Republic.

Randomized controlled trials offer us basic information about effectiveness and safety of drugs. Unfortunately these trials are not able to reveal all drug risks that can even vitally change the therapeutic value of the drug even though there is a selection of patients who enter the study and there are strict conditions for carrying out of these trials. Drug-related problems (DRPs) appear in clinical practice relatively a lot. Non-prescription of drugs that fundamentally decrease mortality, inappropriate drug prescription from the point of view of age or comorbidities, treatment duplicity or non-compliance risk belong among these DRPs.

The target of this study was to describe selected pharmacotherapy risks (particular DRPs) that can appear in everyday clinical practice. We focused on the description of MI secondary prevention with the help of EBM, on opinions, attitudes and experience of general practitioners with generic drugs and generic substitution and on the self-medication of the elderly with the focus on the knowledge and experience with the medicine containing ibuprofen.

### **1. Prescription of EBM to patients in MI secondary prevention by general practitioners in the Czech Republic**

#### **Aim**

The aim was to carry out the analysis of prescription of EBM in patients in MI secondary prevention in the Czech Republic.

## **Methods**

Two studies with similar methodology were carried out. Input data from Atlet project (that monitored the medically preventive care of general practitioners in patients with the high risk of cardiovascular diseases) were used in the first study. All patients after myocardial infarction in anamnesis and with filled complete medication were relegated. Data from electronic documentation of general practitioners (consultants and members of SVL ČLS JEP panel) were used in the second study where all patients in MI secondary prevention were included. Gender, patients' age and the prescription of EBM (beta-blockers, ACEI/ARB, statins, antiplatelet drugs) were observed in both studies. The compensation of cardiovascular diseases risk factors was also observed in the first study and the time period since myocardial infarction was observed in the second one. Statistical analysis of data was carried out in SPSS® 16.0 and PASW® 18.0 software. Parametric and non-parametric statistical tests were used.

## **Results**

1640 patients (1102 men) were involved in both studies. The average age was 66 years in the first study and 71 years in the second one. The frequency of prescribing of main groups of EBM therapy was 75 – 79 % of patients in both studies. The frequency of prescribing was higher (85 – 87 % of patients) in antiplatelet, anticoagulant or combined therapy. About 75 % of patients in MI secondary prevention used at least three out of four EBM drugs. Reduced prescription was recorded depending on patients' age ( $p < 0.05$ ) especially in all particular EBM drugs and their combinations in the second study as well as in beta-blockers and antiplatelet drugs in the first one. No relation to prescription of these groups of drugs depending upon patients' gender was found. Low compensation rate of particular risk factors of cardiovascular diseases was found in the first study. Only about 10 % of patients after myocardial infarction had compensated their blood pressure and total cholesterol to target values.

## **Conclusions**

Our results from both studies show that using EBM therapy after myocardial infarction in the Czech Republic is comparable to other advanced countries, though it is not still optimal similar to the level of compensation of cardiovascular diseases risk factors. It is necessary to focus on improving of the quality of care of these patients because there are a high percentage of patients who are not treated adequately. Professional medical societies of GPs and specialists should play their key roles. Pharmacists and clinical pharmacists should join them as well. Health insurance companies, whose big roles are still not alleged enough, should guarantee quality and accessible care for their clients.

## 2. The analysis of attitudes, opinions and experience of general practitioners with generic drugs and generic substitution in the Czech Republic

### **Aim**

The target was to obtain opinions, knowledge and experienced of general practitioners with generic drugs and generic substitution one year after the introduction of this system in the Czech Republic.

### **Methods**

A 28-item questionnaire which was inspired by similar studies abroad and adjusted for the conditions in the Czech Republic was used for data collection. All general practitioners who took part in the 27<sup>th</sup> National Conference SVL ČLS JEP and in the regional conferences of this professional community from November 2008 to March 2009 were addressed. Statistical analysis was carried out in PASW<sup>®</sup> 18 software. Statistical correlations were tested by selected parametric and non-parametric tests.

### **Results**

263 filled questionnaires were given back (the returnability was 14.3 %). The average respondents' age was  $52.5 \pm 13.7$  years and 67.3 % were females. 37.6 % of respondents considered generic drugs to be bioequivalent to brand name drugs. 46 % of respondents believed that generic drugs are of lower quality than brand name drugs. Only 21.6 % of respondents looked at generic substitution positively. No respondent knew all legal rules of generic substitution implementation. The knowledge of legal rules and attitude towards generic substitution correlated with the respondents' age. The younger respondents had a better knowledge of legal rules ( $p = 0.028$ ) of generic substitution implementation and they had a more positive attitude to it as well ( $p = 0.024$ ). About one fourth of respondents (23.2 %) stated that in the previous month they had faced drug problems that had arisen because of generic substitution. In most cases the dose duplicity in using two drugs with the same active substance and the occurrence of adverse effects in substitution of one drug for another were mentioned.

### **Conclusions**

On the one hand, generic substitution is an instrument that contributes to financial expenses savings for drugs; on the other hand it can bring some risks into patients' pharmacotherapy. In our study we proved a relatively poor knowledge of general practitioners about the principle of the entry of generic drugs to the pharmaceutical market and about the conditions of generic substitution implementation.

Some drug problems within the context of generic substitution implementation were recorded. Some measures that could contribute to the minimization of these risks of these drug-related problems were suggested. Labelling the covers of drugs by international non-proprietary name of active substance would especially belong to these measures as well as the measure of increasing reporting of drug problems arisen in connection with generic substitution. On the basis of these reports a list of interchangeable drugs would be created and updated.

### 3. Risks and safety of self-medication by non-prescription drugs with content of non-steroidal anti-inflammatory drugs with the focus on ibuprofen

#### **Aim**

The aim of this part was to obtain and analyse data about the experience and knowledge of senior citizens with self-medication of pain with the help of non-prescription analgetics with the focus on the ibuprofen active substance.

#### **Methodology**

A cross-sectional study was carried out in retirement communities in Liberecky region and Central Bohemia region. A 19-item questionnaire was used for data collection that took place from April to August 2010. The direct interview with respondents was chosen as the main method. Statistical analysis was carried out in SPSS<sup>®</sup> 16.0 software. Statistical correlations were tested by selected parametric and non-parametric tests.

#### **Results**

9 retirement communities (out of 18 addressed) were involved in the study. 200 senior citizens were included (77 % females, average age  $83 \pm 7$  years), which was 21.7 % of clients of these retirement communities. 64.3 % of respondents suffered from pain almost every day. The muscles and joints were the most common site of pain, followed by back and lower back pain. A large part of respondents used self-medication (45 %). Respondents preferred drugs with the content of ibuprofen (35.9 %) and paracetamol (30.0 %) in self-medication. The use of topical drugs containing non-steroidal analgetics was only minor (1.9 %). The best known effect of ibuprofen was the analgetic one (57.6 %) while only a small part of respondents knew the antipyretic (5.2 %) and antiphlogistic (7.2 %) effects. Younger and more educated respondents had better knowledge of ibuprofen indications ( $p < 0.05$ ). Knowledge of adverse effects and interactions of ibuprofen were on a low level. 57.8 % of respondents replied that they had not known about the adverse effects of ibuprofen. 16 % of respondents thought that there were not any adverse effects of ibuprofen and only 9 % of them knew about serious adverse effects. Older respondents considered adverse effects of ibuprofen as less serious ( $p = 0.017$ ). Similarly the knowledge of interactions of ibuprofen was very low because 84 % of respondents did not know about any particular interactions.

## **Conclusions**

Data from our study confirm results of few previous studies that the knowledge of OTC drugs is generally poor. Although most respondents suffered from pain almost daily and ibuprofen was most often used analgetics, the major part of respondents had not been aware of the fact that ibuprofen was connected with some drug-related problems (adverse effects, interactions). Senior citizens are a part of population which pharmaceutical care should focus on especially because of polymorbidity, polypharmacotherapy and the frequent use of OTC drugs. This part of population had better choose paracetamol and local formulated drugs NSAIDs. Pharmacists or pharmaceutical assistants should guarantee safe and effective self-medications and should try to minimize the occurrence of drug-related problems.